Complete Summary

GUIDELINE TITLE

Guidelines on diagnosis and management of acute pulmonary embolism.

BIBLIOGRAPHIC SOURCE(S)

Guidelines on diagnosis and management of acute pulmonary embolism. Task Force on Pulmonary Embolism, European Society of Cardiology . Eur Heart J 2000 Aug;21(16):1301-36. [373 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Acute pulmonary embolism

GUIDELINE CATEGORY

Diagnosis
Management
Risk Assessment
Treatment

CLINICAL SPECIALTY

Cardiology
Emergency Medicine
Internal Medicine
Obstetrics and Gynecology
Pulmonary Medicine
Radiology
Surgery

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide recommendations for the diagnosis and treatment of acute pulmonary embolism

TARGET POPULATION

Patients at risk for or presenting with pulmonary embolism, including pregnant women

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Clinical presentation and evaluation
    - Assessment of signs and symptoms, such as dyspnea, chest pain, tachypnea
    - Blood gas analysis (evaluation for hypoxemia)
    - Chest x-ray
    - Electrocardiogram
2. Lung scintigraphy (perfusion and ventilation imaging)
3. Pulmonary angiography
4. Spiral computed tomography
5. Echocardiography
6. Detection of deep vein thrombosis
    - Impedance plethysmography
    - Ultrasonography (duplex lower limb real-time B-mode compression ultrasonography or Doppler)
    - Serial leg testing using ultrasonography or impedance plethysmography
7. Measurement of plasma D-dimer levels using enzyme-linked immunosorbent assay (ELISA), traditional latex, and whole agglutination tests

Management

1. Haemodynamic and respiratory support
    - Fluid loading
    - Isoproterenol
    - Dobutamine and dopamine
    - Epinephrine
    - Monitored oxygen therapy
    - Inhaled nitric oxide
2. Thrombolytic treatment
    - Recombinant tissue plasminogen activator (rtPA)

    - Streptokinase
    - Urokinase
3. Surgical embolectomy
4. Anticoagulant therapy
    - Unfractionated heparin
    - Low molecular weight heparins, such as tinzaparin, reviparin
    - Sodium warfarin
    - Acenocoumarol
    - Fluindione
    - Other anticoagulants, such as danaparoid sodium, t-hirudin, and argatroban
    - Monitoring of activated partial thromboplastin time, platelet counts, international normalized ratio (INR), and anti-Xa activity
5. Inferior vena cava (IVC) filters, such as Titanium Greenfield, LGM/Venatech, Simon Nitinol, and Bird's nest filters
    - Use of adjunctive anticoagulant therapy

Diagnosis and treatment in pregnancy

1. Clinical assessment
2. Diagnostic tests
    - Chest x-ray, blood gases, electrocardiogram
    - Arterial oxygen pressure
    - Perfusion lung scan
    - Ventilation lung scan
    - Pulmonary angiography by femoral route
    - Pulmonary angiography by brachial route
    - Spiral computed tomography
    - Plasma D-dimer levels
3. Anticoagulant therapy, including unfractionated heparin and low-molecular-weight heparin, warfarin
4. Thrombolytic agents

MAJOR OUTCOMES CONSIDERED

Diagnosis

- Predictive value of diagnostic tests and assessments

Treatment

- Death rates
- Survival rates
- Recurrent pulmonary embolism rates
- Recurrent venous thromboembolic disease rates
- Recurrent deep vein thrombosis rates

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of evidence:

A. Data derived from multiple randomized clinical trials or meta-analyses
B. Data derived from a single randomized trial or non-randomized studies
C. Consensus opinion of the experts

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The Chairman and seven of the Members of the Task Force on Pulmonary Embolism formed a Core Writing Group (CWG), which included an Editor, responsible for preparation of the final document. The Task Force Members met in September 1998 in Vienna and the Core Writing Group in May 1999 in Warsaw and in January 2000 in Paris. In addition, controversial issues were presented and discussed with the Pulmonary Circulation Group of the European Respiratory Society during an open Workshop organized at the European Respiratory Society annual Congress in Geneva, in September 1998.

Review of the literature and position papers were prepared by the Members according to their area of expertise. Their contributions were then posted on the

Task Force WebBoard and submitted to discussion over the internet. A second phase consisted of preparation and editing of the consecutive versions of the Guidelines by the Core Writing Group, as discussed at the two consecutive meetings as well as over the internet. At the request of the Committee for Scientific and Clinical Initiatives, the Task Force Chairman reported to the Congress of the European Society of Cardiology in August 1999, indicating key points of the emerging guidelines.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Spiral-computed tomography (sCT) seems to be a cost-effective method. A cost-effectiveness analysis based on current scientific literature showed that the five strategies with the lowest cost per life saved (and the five strategies with the lowest mortality) all included sCT angiography. When cost per life saved was the primary outcome parameter, spiral CT angiography of the pulmonary arteries and D-dimer tests provided the lowest cost for work-up of patients with suspected pulmonary embolism (PE). With mortality as the primary outcome parameter, a combination of sCT angiography and an ultrasound study of the legs was the best strategy.

Combining ultrasonography (US) to lung scan and angiography is cost-effective and reduces costs by 5 to 15%, provided ultrasonography is done before lung scan.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guideline document was distributed for correction and endorsement to all Members and independently reviewed for consistency by Internal Reviewers. The document was approved on 14 April 2000.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Excerpted by the National Guideline Clearinghouse (NGC):

<u>Diagnosis</u>

Clinical presentation and clinical evaluation

- Pulmonary embolism has a wide range of clinical presentation.

- A reasonable clinical suspicion is required to avoid missing the diagnosis of pulmonary embolism.
- First line diagnostic tests, such as electrocardiography, chest X-ray and blood-gas analysis are indicated to assess clinical probability of pulmonary embolism and general condition of the patient.
- Clinical evaluation is accurate to discriminate a subgroup of patients with a low likelihood of pulmonary embolism.
- Clinical probability may be estimated empirically or explicitly by a prediction rule.
- Patients with a low clinical probability of pulmonary embolism, no lower limb deep vein thrombosis and a nondiagnostic lung scan have a very low risk of pulmonary embolism.

Lung scintigraphy

- Approximately 25% of patients with suspected pulmonary embolism will have the diagnosis refuted by a normal perfusion lung scan and anticoagulants may be safely withheld.
- Around 25% of patients with suspected pulmonary embolism will have a high probability lung scan and anticoagulant therapy may be instituted.
- The remaining patients will require further diagnostic tests as part of a wider diagnostic strategy.

Pulmonary angiography

- The safety of pulmonary angiography has improved over the past decade.
- Pulmonary angiography is the reference method, but should be reserved for patients in whom non-invasive diagnostic tests remain indeterminate.
- It is safe to withhold anticoagulant therapy in patients with suspected pulmonary embolism and normal angiogram.
- Indirect signs of pulmonary embolism on angiography have not been validated.

Spiral computed tomography

- Spiral computed tomography is more accurate in the demonstration of central or lobar pulmonary embolism than segmental pulmonary embolism.
- A normal spiral computed tomography does not rule out isolated subsegmental pulmonary embolism.
- The safety of withholding anticoagulant therapy in patients with a normal spiral computed tomography angiogram needs further confirmation.

Echocardiography

- Echocardiography is useful in patients with suspected massive pulmonary embolism.
- Whether echocardiography may identify patients who could benefit from thrombolytic therapy in the absence of systemic hypotension or shock remains to be confirmed in prospective studies.

Detection of deep vein thrombosis

- Ultrasonography shows a proximal deep vein thrombosis in 50% of patients with proven pulmonary embolism.
- A normal ultrasonography exam of the leg veins does not rule out pulmonary embolism.
- Serial leg testing may replace angiography in patients with non-diagnostic lung scan findings. However, its practical use seems limited.

Plasma D-dimer levels

- A normal D-dimer level by an enzyme-linked immunosorbent assay (ELISA) may safely exclude pulmonary embolism, provided the assay has been validated in an outcome study.
- Traditional latex and whole agglutination tests have a low sensitivity for pulmonary embolism and should not be used to rule out pulmonary embolism.
- D-dimer is most useful in emergency ward patients. In elderly or inpatients, D-dimer retains a high negative predictive value, but it is normal in less than 10% of patients, and, hence, not very useful.

Treatment

Haemodynamic and respiratory support

- Dobutamine and dopamine may be used in patients with pulmonary embolism, low cardiac index and normal blood pressure.
- Vasopressive drugs may be used in hypotensive patients with pulmonary embolism.
- Monitored oxygen therapy is beneficial in patients with pulmonary embolism and hypoxaemia.
- The usefulness of fluid challenge is controversial and should not exceed 500 ml.

Thrombolytic treatment

- Thrombolytic therapy is indicated in patients with massive pulmonary embolism, as shown by shock and/or hypotension.
- Most contraindications for thrombolytic therapy in massive pulmonary embolism are relative.
- Thrombolytic therapy should be based on objective diagnostic tests.
- The use of thrombolytic therapy in patients with sub-massive pulmonary embolism (right ventricular hypokinesia) is controversial.
- Thrombolytic therapy is not indicated in patients without right ventricular overload.

Surgical embolectomy

- Acute pulmonary thrombectomy has a limited role in massive, life-threatening pulmonary embolism.
- If confirmation of massive central pulmonary embolism prior to surgery can be obtained by echocardiography (preferably transesophageal echocardiography) or spiral computed tomography, angiography is not systematically required.

Anticoagulant therapy

- Patients with pulmonary embolism should be treated with intravenous, weight-adapted unfractionated heparin, with an adjusted activated partial thromboplastin time (aPTT) between 1.5 to 2.5 control (anti Xa activity 0.3–0.6 IU).
- Low-molecular-weight heparin may be used in patients with symptomatic non-massive pulmonary embolism.
- Oral anticoagulant treatment should be initiated during the first 3 days with an overlap with heparin treatments for at least 4 to 5 days. Heparins could be discontinued when the international normalized ratio (INR) has been therapeutic (range 2.0 to 3.0) for 2 consecutive days.
- Patients with a first episode of pulmonary embolism should be treated for at least 3 months if they have a reversible risk factor and for at least 6 months is they have idiopathic venous thromboembolism.
- Oral anticoagulants should be continued for a longer period, possibly indefinitely, in patients with recurrent venous thromboembolism, or continuing risk factors such as cancer.

Venous filters

- Inferior vena cava (IVC) filters are indicated to prevent pulmonary embolism in patients with either absolute anticoagulation contraindications or patients who suffer from recurrent venous thromboembolism despite adequate anticoagulant treatment.
- Inferior vena cava filters are probably indicated after surgical embolectomy.
- Retrievable inferior vena cava filters require further study to validate their use.

Diagnosis and treatment of pulmonary embolism in pregnancy

- An accurate diagnosis is mandatory, as pulmonary embolism requires a prolonged course of heparin in pregnant women.
- All diagnostic modalities, including computed tomography scan and angiography, may be used without a significant risk to the fetus.
- The indication for anticoagulant treatment is the same as in the non-pregnant state.
- Coumarins are formally contraindicated during the first trimester and last 6 weeks of pregnancy.
- Long courses of treatment by unfractionated heparin should be administered subcutaneously.
- Low-molecular heparins are probably safe during pregnancy.

CLINICAL ALGORITHM(S)

A diagnostic algorithm is provided for non-massive suspected pulmonary embolism in emergency room patients.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation. Effort was made to include all relevant evidence relating to the diagnosis and treatment of pulmonary embolism.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Overall

- Improved diagnosis and management of pulmonary embolism, which is a major international health problem. The diagnosis is often difficult to obtain and is frequently missed. Deep vein thrombosis and pulmonary embolism are common causes of illness and death after surgery, injury, childbirth, and in a variety of medical conditions. Nevertheless numerous cases go unrecognized and hence untreated, with serious outcomes.

Specific benefits of anticoagulant therapy

- Mortality in untreated pulmonary embolism is approximately 30%, but with adequate (anticoagulant) treatment this can be reduced to 2-8%.
- Anticoagulant therapy reduces the mortality in patients with pulmonary embolism by 75%.
- The use of low molecular weight heparin may shorten hospital stay and improve quality of life for patients.

Specific benefits of thrombolytic therapy

- The increase in right ventricular afterload observed in patients with massive pulmonary embolism may induce right ventricular failure, systemic hypotension and shock, all associated with a poor outcome. Thrombolytic therapy has beneficial effects on these parameters.

Subgroups Most Likely to Benefit:

Primary and secondary risk factors for venous thromboembolism are summarized in Table 1 of the original guideline document. In general, the incidence rates of deep vein thrombosis and pulmonary embolism increase with age, but this trend may be due to an underlying relationship between age and other co-morbidities, which are the actual risk factors for venous thromboembolism (e.g., cancer, myocardial infarction).

POTENTIAL HARMS

Isoproterenol

- One case report suggests that isoproterenol may be deleterious in patients with pulmonary embolism and shock.

Thrombolytic treatment

- Severe bleeding occurs in 14% of the patients with pulmonary embolism who are receiving thrombolytic therapy after pulmonary angiography, which is twice the rate observed in heparin treated patients. Bleeding at the venous puncture site for angiography represents the first source of bleeding and accounts for 36 to 45% of major haemorrhages. Intracranial bleeding occurs in 1.9% in these patients.

Anticoagulant therapy

- The most common complication of oral anticoagulant therapy is bleeding and the risk is related to the intensity of anticoagulation. The most important non-haemorrhagic side effect of oral anticoagulant therapy is skin necrosis, which may occur during the first week of treatment.
- A loading dose of anticoagulants may be harmful by inducing a temporary hypercoaguable state due to the shorter half-life of proteins C and S compared to other coagulation factors.
- Heparin-induced thrombocytopenia is a rare but life-threatening side effect. The frequency of heparin-induced thrombocytopenia is greater with unfractionated heparin that with low-molecular-weight heparin.

Venous filters

- Filters are prone to complications such as penetration of the wall of the vena cava and caudal migration along with insertion site complications such as deep vein thrombosis and haematomas

Diagnosis and treatment of pulmonary embolism in pregnancy

- Radiation is absorbed by the fetus during diagnostic tests.
- Vitamin K antagonists cross the placenta, and warfarin is associated with a characteristic embryopathy during the first trimester. Its administration in the third trimester can also result in fetal and neonatal haemorrhage and placental abruption. Although warfarin may be associated with central nervous system anomalies in any trimester in pregnancy, that risk is very low.
- The overall incidence of bleeding with thrombolytic agents is about 8% (usually from the genital tract and often severe.)

CONTRAINDICATIONS

CONTRAINDICATIONS

Pulmonary angiography

- Contraindications include allergy to iodine containing contrast agents, impaired renal function, left bundle branch block, severe congestive heart failure, and severe thrombocytopenia. Severe pulmonary hypertension (mean pulmonary artery pressure >40mmHg) increases the risks of complications, but by reducing amounts of contrast and increasing linear rise this is well within reasonable limits.

Anticoagulant therapy

- Contraindications include active bleeding, haemostatic disorders, severe uncontrolled hypertension and recent surgery.
- The use of unfractionated heparin and low-molecular-weight heparin is contraindicated in patients with heparin-induced thrombocytopenia and starting oral anticoagulants without another immediately active anticoagulant may be hazardous.
- The monitoring of anti-Xa activity in elderly patients and those with chronic renal failure has been advocated, but this remains controversial.
- During pregnancy, oral anticoagulants cross the placenta and are responsible for abortion and embryopathies during the first trimester. Coumarins are formally contraindicated during the first trimester and last 6 weeks of pregnancy.

Thrombolytic therapy in patients with massive pulmonary embolism

- Absolute contraindications to thrombolytic therapy include active internal bleeding and recent spontaneous intracranial bleeding.
- Relative contraindications include major surgery, delivery, organ biopsy or puncture of non-compressible vessels within 10 days; ischaemic stroke within 2 months; gastrointestinal bleeding within 10 days; serious trauma within 15 days; neurosurgery or ophthalmologic surgery within 1 month; uncontrolled severe hypertension (systolic pressure >180 mmHg, diastolic pressure >110 mmHg); recent cardiorespiratory resuscitation; platelet count <100,000 mm^3; prothrombin time <50%; pregnancy; bacterial endocarditis; diabetic hemorrhage retinopathy.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Guidelines on diagnosis and management of acute pulmonary embolism. Task Force on Pulmonary Embolism, European Society of Cardiology . Eur Heart J 2000 Aug;21(16):1301-36. [373 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000 Aug

GUIDELINE DEVELOPER(S)

European Society of Cardiology - Medical Specialty Society

SOURCE(S) OF FUNDING

The Guidelines were developed with the help of a budget assigned to the Task Force by the European Society of Cardiology and without the involvement of any commercial organization.

GUIDELINE COMMITTEE

Task Force on Pulmonary Embolism, European Society of Cardiology (ESC)

European Society of Cardiology's Committee for Practice Guidelines and Policy Conferences

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Task Force on Pulmonary Embolism, European Society of Cardiology (ESC): Core Writing Group: A. Torbicki (Chairman), E. J. R. van Beek (Editor), B. Charbonnier, G. Meyer, M. Morpurgo, A. Palla, A. Perrier

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

An update is not in progress at this time.

GUIDELINE AVAILABILITY

Electronic copies: Available from the European Society of Cardiology (ESC) Web site.

Print copies: Available from Elsevier Publishers Ltd. 32 Jamestown Road, London, NW1 7BY, United Kingdom. Tel +44.207.424.4200/ Tel: +44 207 424 4389; Fax: +44 207 424 4433; e-mail: gr.davies@elsevier.com; Web site: www.escardiocontent.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Recommendations for Task Force creation and report production. Sophia Antipolis (France): European Society of Cardiology, 2002.

Electronic copies: Available in Portable Document Format (PDF) from the European Society of Cardiology (ESC) Web site.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on September 17, 2001. The information was verified by the guideline developer on September 27, 2001.

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